

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re application of: **Malin ERNEBRANT et al.**

Application No.:	10/591,233	Art Unit:	1616
§371 date:	July 5, 2007	Examiner:	Abigail Fisher
		Confirmation No.:	9327

DECLARATON PURSUANT TO 37 CFR 1.132

1. I, Malin Ernebrant, declare THAT:
2. I am a Swedish citizen, residing at Sjöströms väg 7, 275 61 Blentarp, Sweden.
3. I have been employed by Gambro Lundia AB since 01.09.2002, and am currently a Project leader.
4. I have carried out research on medical devices and drugs, and especially on bicarbonate buffered solutions in such products, during my time of employment at Gambro.
5. I am a co-inventor of the invention set forth in United States Patent Application No. 10/591,233 filed on February 22, 2005 entitled "A MEDICAL SOLUTION, A METHOD FOR PRODUCING SAID MEDICAL SOLUION AND USE THEREOF". The publication of the application (2007/0298125) is enclosed as Exhibit 1.
6. I have performed the following experiments in order to prove stability and repeatability of pH in bicarbonate buffered solutions.

MATERIALS AND METHODS

7. The two separate concentrates were prepared respectively, by mixing required chemicals and milli Q water (see table 1 below). Four separate sets of concentrates were prepared. The electrolyte composition of each concentrate can be found in table 2 in section 9.

BiC concentrate	Volume(l)	0,25	
	conc (M)	mass (g)	
NaHCO ₃	1,39E-01	2,92	
Na ₂ CO ₃	6,61E-01	17,51	
NaCl	-----		
Acid part	Volume (l)	4,75	
	conc (M)	mass (g)	
HCl	3,84E-02	182,400	MI
NaCl	7,05E-02	19,57	
CaCl ₂ *2 H ₂ O	1,84E-03	1,28	
MgCl ₂ *6H ₂ O	5,30E-04	0,51	

Table 1: Mixing of concentrates

	Acid part	BiC part	Mix
	mM	mM	mM
Na ⁺	70,50	1461,00	140,03
Cl ⁻	113,64	0,00	107,96
Ca ²⁺	1,84	0,00	1,75
Mg ²⁺	0,53	0,00	0,50
HCO ₃ ⁻	0,00	139,00	6,95
CO ₃ ²⁻	0,00	661,00	33,05

Table 2: Ionic strength in each solution

8. pH was measured in each concentrate, as well as in mixed solutions. The concentrates were mixed, one part of the bicarbonate concentrate and 19 parts of the acid concentrate in order to obtain a solution with final concentrations according to the table below. Three separate mixings were performed for each set of concentrates.
9. When preparing the solutions, target pH of reconstituted solutions was set to 7,25.
10. In one set of experiments, the bicarbonate concentrate was placed in open containers, and pH measured during 17 days.
11. In another set of experiments, both concentrates were stored at 30°C, pH was measured in the concentrates as well as in reconstituted solutions during one month.

RESULTS

12. pH was measured in each mixing.

Preparation	1	2	3	4
Mix 1	7,25	7,19	7,29	7,24
Mix 2	7,25	7,22	7,22	7,22
Mix 3	7,29	7,23	7,3	7,25
Mean	7,26	7,21	7,27	7,24
Stdev	0,02	0,02	0,04	0,02

Table 3: pH measurements

13. The bicarbonate concentrate, which traditionally is the one sensitive to pH changes, was placed in open containers and pH was measured during 17 days. Only small changes were observed.

BiC	day 0	day 1	day 2	day 7	day 10	day 16	day 17
1:20	10,32	10,26	10,26	10,26	10,2	10,24	10,25

Table 4: pH measurements in bicarbonate concentrate in open containers

14. To provide additional stability data, two sets of bicarbonate and acid concentrates were stored in 30 °C for 31 days. pH in each concentrate was measured according to the table below. At each measurement, solutions were mixed and pH measured. Target pH in this set of experiments was set to 7,2.

Ph							
1 st set	day 0	day 3	day 7	day 10	day 24	day 31	
Acid	1,22	0,75	1,03	1,07	1,13	1,03	
BiC	10,34	10,35	10,29	10,34	10,41	10,32	
Mix	7,11	7,09	7,07	7	7,09	7,17	

2 nd set	day 0	day 3	day 7	day 10	day 24	day 31	
Acid	1,18	0,74	1,02	1,05	1,13	1,01	
BiC	10,34	10,31	10,25	10,32	10,37	10,3	
Mix	7,16	7,12	7,08	7,07	7,19	7,16	

Table 5: one month stability of concentrates

CONCLUSION

15. Target pH is obtained with good accuracy at each occasion. pH in the bicarbonate concentrate remains stable also when stored in open containers which by no means limit CO₂ exchange with the atmosphere. pH also remains stable in the acidic concentrate. The stable pH of the two concentrates over time also secures obtaining of target pH over time.
16. I hereby declare that all the statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further, that these statements are made with the knowledge that wilful false statements are so made punishable by fine or imprisonment, or both, under Section 101 of Title 18 of the United States Code and that such wilful false statements may jeopardize the validity of the application of any patent issuing thereon.

2011-01-17
Date

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